Upper Limb Disorders in Cancer Survivors
A Musculoskeletal Medicine Perspective

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Objectives

- Overview of common neuromuscular disorders encountered in cancer rehab based on region
- Review Various Treatments
- Tissue Healing Review
- Overall Musculoskeletal Rehabilitation Approach
- Provide a framework for a rehabilitation prescription that enables cancer patients to return to their usual activities.

Cancers Commonly Leading to Upper Limb Disorders in Cancer Patients and Survivors

- Breast
- Sarcoma
- Head and Neck
- Non-Hodgkins Lymphoma
- Other Non-Solid requiring BMT (GvHD)

Pain Overview

Nociceptive	vs	Neuropathic
• Pain that arises from a stimulus that is outside of the nervous system • Proportionate to the stimulation of the receptor • When acute serves a protective function		• Pain initiated or caused by a primary lesion or dysfunction in the nervous system • No nociceptive stimulation required • Disproportionate to the stimulation of receptor • Other evidence of nerve damage

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Upper Limb Pain In Cancer Patients and Survivors
General Etiology

- Nociceptive Somatic
  - Musculoskeletal
    - Arthritis/Degenerative
    - Rotator Cuff Tendonitis
    - Adhesive Capsulitis
    - Med/Lat Epicondylitis
    - De Quervain's Tenosynovitis
    - Post-surgical Pain
    - Myofascial
    - Fracture/Impeding Fracture
    - Bony Metastasis
  - Integumentary
    - Cellulitis
  - Vascular
    - Post-operative Swelling
    - Lymphedema
    - Cording/Thrombophlebitis
    - Thromboembolism
- Neuropathic
  - Central
    - Thalamic
    - Funicular
  - Peripheral
    - Radiculopathy
    - Plexopathy
    - Neuropathy
    - Post-mastectomy Syndrome
  - CRPS

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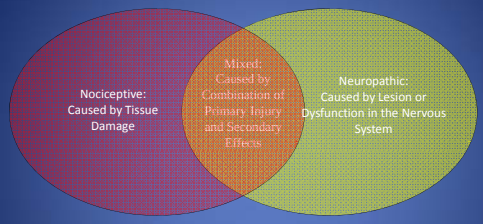
Upper Extremity Pain in Breast Cancer
Overlap of Nociceptive and Neuropathic Pain



- Arthritis
- Mechanical Low Back Pain
- Sports/exercise Injuries
- Postoperative Pain

- Low Back Pain
- Fibromyalgia
- Cancer Pain

- Thalamic Pain
- Funicular Pain
- Radiculopathy
- Plexopathy
- Neuropathy

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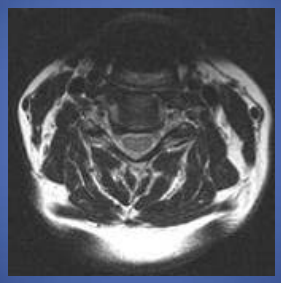
Upper Limb Pain Neuropathic Origin

C-5 Disk Herniation



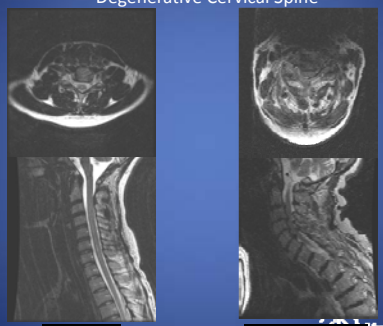
Upper Limb Pain Neuropathic Origin

Causes of Radiculopathy

- Arthritis
- Disk Disease
- Spinal Stenosis
- Spondylolisthesis
- Fracture
- Cancer

Upper Limb Pain Neuropathic Origin

Degenerative Cervical Spine

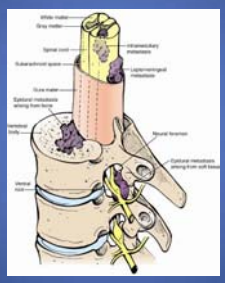


Normal

Degenerative

Upper Limb Pain Neuropathic Origin

Axial Spinal Tumors



From: Principles & Practice of Cancer Rehabilitation. Stubblefield M and O'Dell M, editors. Demos Medical Publishing, New York. 2009.

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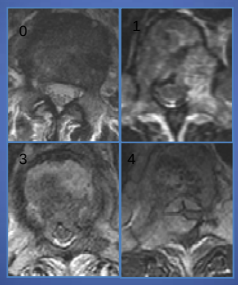
Upper Limb Pain Neuropathic Origin

Epidural Spinal Cord Compression



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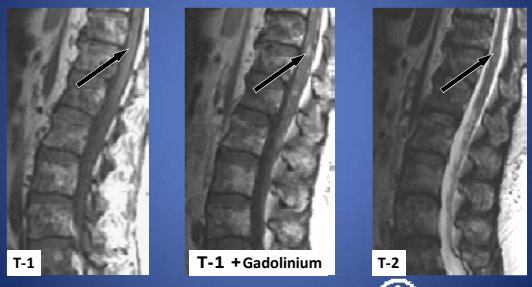
Upper Limb Pain Neuropathic Origin

Leptomeningeal Disease



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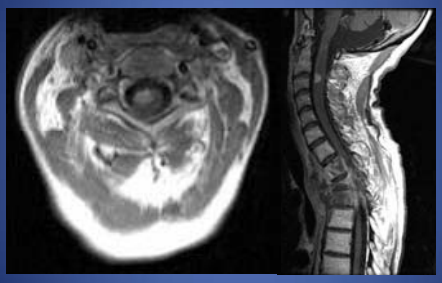
Upper Limb Pain Neuropathic Origin

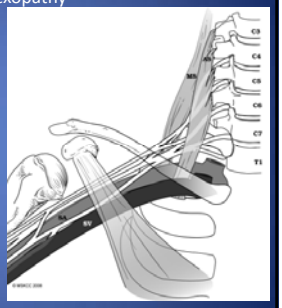
Intramedullary Metastasis



Upper Limb Pain Neuropathic Origin

Causes of Plexopathy

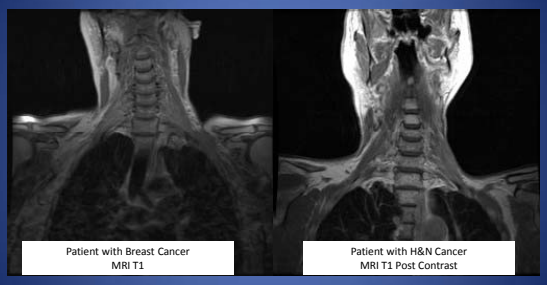
- Idiopathic
  - Parsonage Turner Syndrome
- Chemotherapy
- Radiation
- Traumatic
- Malignant



From: Lewis J, Krol G. Principles of Plexus Imaging. In: Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009, 149-160.

Upper Limb Pain Neuropathic Origin

Tumor vs. Radiation Plexopathy



Patient with Breast Cancer
MRI T1

Patient with H&N Cancer
MRI T1 Post Contrast

From: Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009.

Upper Limb Pain Neuropathic Origin Causes of Neuropathy

- Chemotherapy
- Compression
- Critical Illness
- Idiopathic
- Infection
- Inherited
- Paraneoplastic
- Paraprotein
- Toxic/Metabolic
- Trauma
- Vasculitis

Upper Limb Pain Neuropathic Origin Neurotoxic Chemotherapeutics

- Vinca alkaloids
- Taxanes
- Platinum-based Compounds
- Etoposide
- Cytarabine
- Suramin
- Thalidomide
- Epothilone
- Bortezomib
- Interferon-alpha
- Capecitabine

Taxanes

(paclitaxel, docetaxel)

- From Pacific Yew Tree (*Taxus brevifolia*)
- Indications:
  - Solid tumors (ie, ovarian and breast cancer)
- Mechanism of action:
  - Binds tubulin and blocks its polymerization into microtubules
  - Arrests mitosis in metaphase
- Clinical Features:
  - Distal symmetric sensorimotor axonal PN
  - Affects large fiber > small fiber functions

Platinum Based Compounds

cisplatin (Platinol AQ®), carboplatin (Paraplatin®), oxaliplatin (Eloxatin®)

- Indications:
  - Solid tumors (ie, ovarian, testicular, & bladder cancer)
- Mechanism of action:
  - Binds and cross-links DNA, inhibits protein synthesis, and impairs axonal transport
- Clinical Features:
  - Preferential damage to dorsal root ganglion
  - Distal symmetric predominately sensory axonal PN
  - Affects large fiber > small & sensory > motor fibers
  - Sensory ataxia
  - Symptoms can appear after treatment and progress for months following treatment

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Capecitabine

(Xeloda)

- Oral fluoropyrimidine carbamate
- Metabolized to 5-FU
- Efficacy in breast and colorectal cancer
- Associated with Hand-foot Syndrome
  - AKA, "chemotherapy-induced acral erythema"
  - AKA, "palmoplantar erythrodysesthesia"
  - 68% with 10% developing grade 3 toxicity
- Associated with Small-fiber Neuropathy

Stubblefield MD, Custodio CM, Kaufman P, Dickler MN. Small-fiber neuropathy associated with capecitabine (Xeloda) induced hand-foot syndrome: a case report. J Clin Neuromusc Dis. 2006;7:128-32.

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Upper Limb Pain Neuropathic Origin Clinical Features of Hand-Foot Syndrome

- Palmar and plantar
  - Dysesthesias
  - Pain
  - Paresthesias
  - Swelling
  - Erythema
  - Hyperpigmentation

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Musculoskeletal Pain

- Nociceptive Somatic
  - Musculoskeletal
    - Arthritis/Degenerative
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    - Post-surgical Pain/Scar Formation
    - Myofascial
    - Fracture/Impeding Fracture
    - Bony Metastasis

Musculoskeletal (Nociceptive)Pain In Cancer Patients

Potential Causes

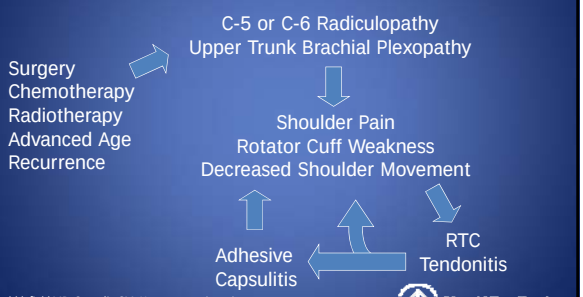
- Deconditioning- Muscle atrophy, stiffness, poor aerobic capacity
- Intrinsic healing ability- Too much or too little scar tissue formation, too much or too little inflammation.
- Baseline physical condition
- Complications of cancer treatment- Surgery, Chemotherapy, Radiation.

Shoulder

- Primary Compressive Disease
  - –Impingement
    - Arises from abnormal GH mechanics leading to superior migration of humeral head into CA arch.

Upper Extremity Pain in Breast Cancer

The Shoulder Pain Cycle



Stubblefield MD, Custodio CM. Upper-extremity pain disorders in breast cancer. Arch Phys Med Rehabil. 2006;87(3 Suppl):96-9.

Shoulder

Rotator Cuff Disease

- Need sufficient RTC strength to maintain glenohumeral balance.
- Tight anterior muscles and weak posterior muscles contribute to imbalance.

Shoulder Disorders in Breast Cancer Patients/Survivors

Shoulder Complaints from time of surgery to 6 years post op

ROM	PAIN	LOSS of FUNCTION
10-55%	22-38%	42-56%

SHAMLEY D, LASCURAIN-AGUIRREBEÑA I, OSKROCHI R, SRINAGANATHAN R. Shoulder morbidity after treatment for breast cancer is bilateral and greater after mastectomy. *Acta Oncologica,* 2012; Early Online: 1–9

Shoulder

- **Adhesive Capsulitis**
  - Pain and restricted GH motion
  - Common post chest and or breast surgery
  - Prolonged immobilization is RF
    - Phases
      - 1) Painful
      - 2) Stiffening
      - 3) Thawing

Myofascial Pain Causes

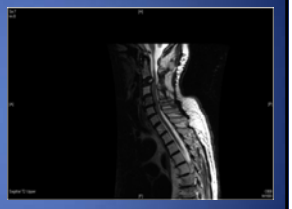
- Deconditioning
- Immobility
- Scar Tissue Formation
- Altered Body Mechanics
- Hormonal Therapies

Myofascial Pain

- Case

68 year old male with Hurthle Cell thyroid CA with metastases to spine and pelvis including C3, T5, L1,L3, L5, right acetabulum.

Past Tx: Thyroidectomy, Modified Radical Neck Dissection
External Beam RTX, Radioactive Iodine, T3 laminectomy/fixation T3-T5.



Myofascial Pain

- Case

Sudden onset severe mechanical radicular cervical Pain secondary to C3 Burst Fracture underwent decompression surgery C2-C5 fusion with allograft

Myofascial Pain

- Case
- Unremarkable immediate post operative course.
- Limited C-spine and shoulder ROM, constant left sided posterior neck/shoulder pain, worse since stopping Pre-gabalin.
- Pain to palpation, hypertonicity, spasm.

Myofascial Pain

Treatment

Trigger point injections to left trapezius, levator scapula, and cervical paraspinal muscles.

Dry needling technique using 30 G I inch needle 1 mL of Pilocarpine 10mg/mL injected in to 10 different points .

Degenerative Musculoskeletal Conditions in Cancer Patients

Is this population more vulnerable?

- Chronic nature of cancer
- Lifestyle Factors
- Obesity

Cancer and Degenerative Musculoskeletal Conditions

- Prolonged period of immobilization
- Toxicity from CTX and RTX
- Deprivation of Physical Activity/Exercise
- Altered Biomechanics post surgery

Cancer Treatment Leading to Muscle Atrophy and Deconditioning.

Androgen Deprivation Treatment (ADT)

- Prostate cancer is dependent upon androgen initially for its continued growth.
- Androgen production occurs primarily in the testes.
- Testicular production of androgen is regulated by the hypothalamic pituitary axis.
- The adrenal glands produce the remainder of the circulating androgens.

Cancer Treatment Leading to Muscle Atrophy and Deconditioning

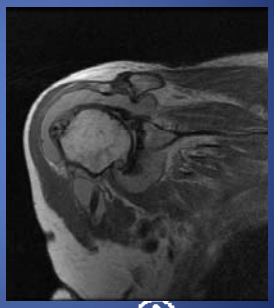
Androgen Deprivation Treatment (ADT)

- GnRH agonists significantly decrease lean body mass and increase fat mass.
- Most of the fat accumulation is subcutaneous adipose tissue.
- The decrease in lean body mass (sarcopenia) and increase in fat mass appear to begin within the first year, although some further decrease in muscle mass may be seen for at least three years.

Alibhai SM et al. Impact of Androgen Deprivation Therapy on physical function and quality of life in men with non-metastatic prostate cancer. J Clin Oncol 2010;28:5038.

Shoulder

- Osteoarthritis
  - AC joint most common
  - GH second most common
  - Progressive Loss of articular cartilage
  - Loss of ROM
  - Effusion
  - Transient Synovitis



Elbow

- Lateral
  - Lateral Epicondylitis
  - OCD
  - Fractures (radial head, capitellum)
  - Nerve entrapment (ulnar, radial, median)
- Medial
  - Medial Epicondylitis
  - Fractures
- Posterior
  - Olecranon Bursitis
- Diffuse
  - Biceps Tendon Rupture
  - Tumor
  - Referred Pain
  - OA
  - Synovitis

Wrist

- Conditions Common in Cancer Patients and Survivors
  - OA
  - AVN (Kienbock's disease)
  - Nerve Entrapment (CTS, Ulnar tunnel syndrome)
  - **Repetitive Sprain Likely Most Common**
    - DeQuervain's Disease
    - FCU/FCR tendinitis
    - ECU Subluxation and Tendinitis
    - Intersection Syndrome

Hand

- Conditions Common in Cancer Patients and Survivors
  - OA
  - Tenosynovitis
  - AI Induced Arthralgias
  - Trigger Finger
  - Boutonniere deformity
  - Swan-neck deformity

Nerve Entrapment In The Upper Limb And Cancer

- Lymphedema
- Encountered after radiation
- Scar Tissue Formation
- Overuse

Carpal Tunnel Syndrome Related to Lymphedema After Breast Cancer Treatment

- Ganel A et al. *Nerve entrapments associated with postmastectomy lymphedema.* Cancer. 1979 Dec;44(6):2254-9.
- 90 females post mastectomy for breast CA.
- Lymphedema found in 50% of these patients.
- 28% of the patients has CTS,
- Compared with 8% on the nonoperated side.

Carpal Tunnel Syndrome and Lymphedema Secondary to Breast Cancer Treatment

- Case

66 y/o female PMHx right sided breast cancer T4N1 ER/PR neg disease diagnosed in 1997 treated with

-Surgery- right sided modified mastectomy, Axillary Lymph Node Dissection

-CTX- Adriamycin, Cytoxan, Taxol (ACT)

-RTX- External Beam Radiation Treatment – 5040 cGy to anterior chest wall, 5040 cGy to supraclavicular fossa.

Carpal Tunnel Syndrome and Lymphedema Secondary to Breast Cancer Treatment

- Case

NCS- Right Median/APB motor- Dec. Amp, Prolonged onset latency. Right Median Sensory D2-Dec. Amp

Needle EMG-Inc. Amp/Duration

No evidence for PPN or Brachial Plexopathy

Ultrasound Exam- Heterogenous median nerve measuring 22 mm

Median Nerve Hydrodissection

- Smith et al-
  - Ulnar Approach
  - Hydrodissect above and below median nerve
  - 2 mL of medication

Modification

  - Abx prophylaxis given
  - Sterile conditions

Smith J, Wisniewski SJ, Finnoff JT, Payne JM. Sonographically guided carpal tunnel injections: the ulnar approach. J Ultrasound Med. 2008 Oct;27(10):1485-90

Median Nerve Hydrodissection

Ulnar Nerve Entrapment

- Cubital Tunnel Syndrome
  - Lymphedema
  - Tumor
  - Chemotherapy
  - Radiation Therapy
  - **Repetitive Strain**
- Ulnar (Guyon's) Tunnel Syndrome
  - Same Etiologies as Cubital Tunnel Syndrome
  - Can occur from crutch use

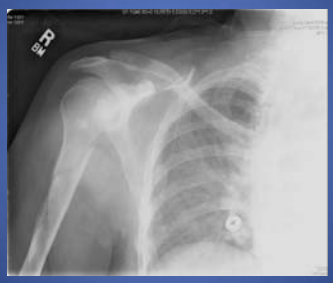
Malignant Shoulder

Mirels Criteria

Variable	SCORE 1	2	3
PAIN	MILD	MODERATE	FUNCTIONAL
LOCATION	UPPER LIMB	LOWR LIMB	PERITROCHANTERIC
SIZE	LESS THAN 1/3	1/3 TO 2/3	GREATER YHAN 2/3
NATURE	BLASTIC	MIXED	LYTIC

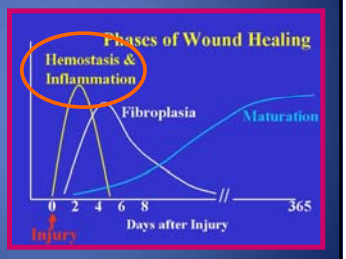
Mirels H. Metastatic disease in long bones: a proposed scoring system for diagnosing impending pathologic fractures, Clin Orthop Relat Res. 1989;249:256-264

Upper Extremity Pain in Breast Cancer Pathologic Fracture



MSK REHABILITATION
Tissue Injury & Repair Phases

- Inflammation
- Repair
  - Fibroplasia
  - Hyperplasia
- Maturation
  - Remodelling



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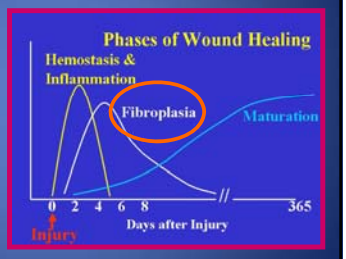

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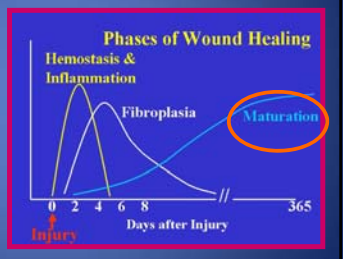

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MSK REHABILITATION
Phase I: Injury & Inflammation

- **Lasts days**
- **Bleeding & Hemostasis**
- **Inflammation**
  - **Edema**
  - **Pain**
  - **Warmth**
  - **Redness**
  - **Dysfunction**

MSK REHABILITATION
Phase I: Injury & Inflammation

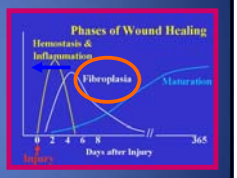
- Inflammation
  - Essential for repair
  - Short lived in most cases
    - Injury site & severity
    - Tissue type injured
    - Patient factors
  - Too much/too long ➔ bad
  - Too little/too short ➔ bad
    - E.g. Chronic tendinopathy

MSK REHABILITATION
Phase II: Fibroplasia/Repair

- **Lasts 6-8 weeks**
- **Cell proliferation**
  - **Growth factor release**
  - **Fibroblast proliferation**
    - **➔Type III collagen**
- **Granulation tissue forms**
  - **Fibroblasts**
  - **Type III collagen**
  - **Neovascularization**

MSK REHABILITATION
Phase II: Fibroplasia/Repair

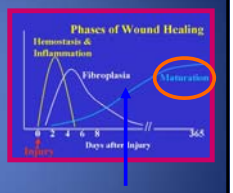
- Tenuous time
  - Appearance > function
  - Risk re-injury / regression
- Graded rehabilitation
  - Criterion based
  - Education
    - Patient, Parents, Coach
  - Monitor for regression
- Most RTP during this period



"Bad Drywall Job"

MSK REHABILITATION
Phase III: Maturation/Remodeling

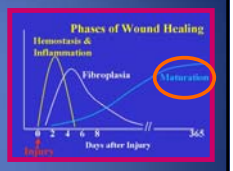
- Lasts for months
- Maturation of tissue
  - Type III → Type I collagen
  - Realign & remodel fibers
    - Force magnitude
    - Force direction
  - Reduced cellularity
  - Reduced vascularity
- Scar tissue → never normal



Failure to progress = tendinopathy

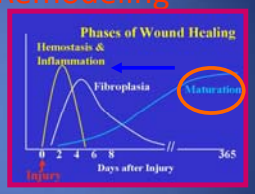
MSK REHABILITATION
Phase III: Maturation/Remodeling

- Clinically
  - Muscle imbalances
    - Motion
    - Strength / Endurance
  - Kinetic chain dysfunction
  - NMC Deficits
  - Technique alterations
  - → often subtle
- Risk re-injury

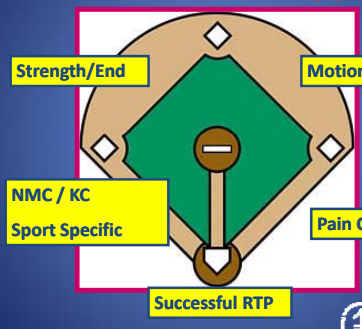


MSK REHABILITATION
Phase III:
Maturation/Remodeling

- Rehabilitation
  - ID & Rx deficits
  - Monitor for trouble
    - Peformance
    - Recovery
    - Pain
    - Swelling
  - Education
- If regress, treat accordingly



MSK REHABILITATION
Baseball Diamond Approach

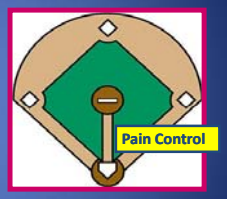


MSK REHABILITATION
Pain Control

- Control pain & inflammation
- PRICE
  - Protect (vs long immob)
  - Relative rest
  - Ice
  - Compression (not too much)
  - Elevation (above heart)
- Special cases = quad contusion

MSK REHABILITATION
Pain Control - Medications

- Analgesics
  - Acetaminophen
  - Tramadol/Narcotics
- Anti-inflammatories
  - NSAIDs
    - Analgesic +
    - Anti-inflammatory?
    - May impair healing
  - Not corticosteroids

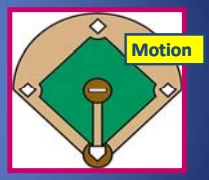


MSK REHABILITATION
Pain Control - Modalities

- Heat → generally bad
  - US = heat
- Ice → generally good
- Electrical (e.g. "stim")
  - Possibly beneficial
    - Anti-edema
    - Analgesic
  - Data mixed

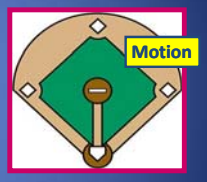
MSK REHABILITATION
Motion

- Pain control precedes motion
- Benefits
  - Anti-nociceptive
  - Anti-edema (at right dose)
  - Initiates NMC training
    - Strength/Endurance
    - Higher level functions
  - Promotes tissue healing
  - Mentally gratifying (→ function)



MSK REHABILITATION
Motion

- Type of motion
  - Passive (PROM)
  - Active assisted (AAROM)
  - Active (AROM)
  - Resisted (RROM)
- Rx dictated by:
  - Healing phase
  - Injury specifics
  - Pain control



MSK REHABILITATION
Motion

- Beware PROM in acute joint
  - Increased pain
  - Increased inflammation
  - Potential damage
- AAROM → AROM → RROM
  - Control motion arc
  - Control forces
- Usually still in Phase II → treat accordingly
  - Monitor for regression

MSK REHABILITATION
Motion - Stretching

- Static
  - Manual
    - 3-5 reps 30-60 sec
  - Splint – gentle, prolonged
- Proprioceptive NM Facilitation
  - Contract-relax (CR)
  - Contract-relax, agonist contract (CRAC)
  - Possibly more efficient acute gain in ROM
  - Usually requires another person
- Ballistic – generally not

MSK REHABILITATION
Strength / Endurance

- Remember goal
- Adequate fxn strength/end
- Specific for:
  - Range of motion
  - Contraction type
  - Speed
  - Energy system
  - Movement pattern

MSK REHABILITATION
Strength / Endurance - Isometric

- No intentional joint motion
- Muscles co-contract
  - E.g. 6 sec co-contractions
  - 5-10 reps
- Can start early
  - Even in splint/case
- May reduce pain, edema, & atrophy
- Role in increasing strength & mass?
- Multi-angle - 15 degrees either direction

MSK REHABILITATION
Strength / Endurance - Isotonic

- Muscles changing length
  - Concentric – shortening
  - Eccentric – lengthening
    - Carryover ECC → CON
- Need pre-requisite motion
- Usually implemented as AROM
  - Add resistance of choice later (RROM)
    - Issue of elastic resistance
  - Consider % increase in load – e.g. Cuff

MSK REHABILITATION
Strength / Endurance - Isotonic

- More stressful
  - Higher resistance
  - Eccentrics
  - Higher speeds
  - Terminal motion arcs
  - More reps ➔ fatigue
  - More joints – juggling balls
- Manipulate strength/end parameters as clinical condition (e.g healing phase) dictates, with the ultimate goal in mind

MSK REHABILITATION
Strength / Endurance - Isokinetic

- Control contraction speed
  - Speed often not functional
- Training benefits?
- May exacerbate symptoms
- Quantitative benefits
  - Can detect & monitor speed specific deficits both ECC & CON
  - Research

MSK REHABILITATION
NMC / Kinetic Chain / Sports

- Neuromuscular Control
  - Afferent = proprioceptive
  - Efferent = muscle ctx
  - Coordination aff => eff
- Strength doesn't guarantee good NMC
  - Proprio deficits despite nl strength
  - Poor movement despite nl strength

MSK REHABILITATION
NMC / Kinetic Chain / Sports

- Detect deficits
  - Assess balance
  - Assess movement patterns
  - Sport-specific scenarios
- Training Continuum
  - AROM, Wobble boards, foam rollers
  - Rhythmic stabs, body blades
  - Plyometric training
    - Jumps, hops, etc.
- Motion, Speed, Energy specificity

MSK REHABILITATION
NMC / Kinetic Chain / Sports

- Build movement patterns into sports specific motions
- Graduated return to sports
  - Appropriate monitoring
  - Post-RTP rehab
  - Monitor for problems

MSK REHABILITATION
Around the Horn

- Constantly consider
  - What is needed to RTP?
  - Where are they in healing?
    - Is there regression?
    - "Tagged out at second"
- "The double steal"
  - Can address motion, strength, endurance, & NMC simultaneously

MSK REHABILITATION

Around the Horn

- **Importance of core**
  - Component of all phases
  - Integrate throughout
- **Conditioning**
  - Energy system specificity
  - Integrate throughout
- **Technique**
  - Before vs after injury
  - Don't wait until you're on your way home.

The Kinetic Chain

- Takes into consideration the biomechanical and physiologic contributions of distant body segments.
- Distant segment contributions key to the sequential activation necessary to accomplish activity.
- Sequential activation=Kinetic Chain

KINETIC CHAIN-WHAT IS IT?

- Nicholas JA et al (1977)
  - Originally described the **link theory** in which the ankle, knees and hips act as a link system making possible the **transmission of forces** from the legs into the pelvis and spine during running, jumping, kicking and throwing.

KINETIC CHAIN-WHAT IS IT?

- More recently the kinetic chain has been described as the **sequencing** of individual body **segments** and **joints** to accomplish a task
  - Throwing a ball
  - Swinging a golf club
  - Bench pressing
  - Using Broom
  - Shoveling Snow
  - Lifting Children

KINETIC CHAIN-WHAT IS IT?

- In a throwing athlete, most of the throwing power is generated by a **complex sequence of activation** which begins in the **lower limbs** and translates through the the **hips, trunk** and **core musculature** to the **arm** and finally the **terminal link** (or hand) for the eventual release of energy

KINETIC CHAIN-WHAT IS IT?

- **51%** of the total **kinetic energy** and **54% force generated** in the tennis serve are created by the lower legs, hips and trunk Kibler WB (1995)
- The largest proportion of energy and force in this throwing **sequencing** is derived from **larger, proximal segments** Kibler WB (1995)